THE HUXLEY LECTURE.

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THE ADVANCE OF MEDICAL SCIENCE SINCE HUXLEY'S DAY.

Huxley died in 1895. It is difficult nowadays for young people to realise how powerful was his influence in 1902, when I became an undergraduate at Cambridge, and probably it was even then beginning to decline. As far as I was concerned this influence was profound, as is illustrated by the fact that the first prize I obtained at Cambridge was invested in the purchase of all his essays. In those days it was customary for undergraduates to discourse on topics that interested them before various societies—a practice which I regret to hear has now almost ceased, undergraduates preferring to listen to dons rather than run their own societies. I have recently read again, after thirty years, some of my own undergraduate efforts. I am impressed and rather surprised to see how greatly influenced I must have been by Huxley's writings. In one case I find I even stole a title from him, and called a paper " Science and Culture," although I must add I am relieved to see that I did not crib any substantial part of his famous article on this subject. Another paper, entitled " Sin," centred round two discourses that influenced me at that time: one was Huxley's " Evolution and Ethics," and the other a lecture given by a Professor of Theology on the " Fall of Man." Opinion on theological problems in those days, especially when unorthodox, was a much more serious matter than it is nowadays, and my views on Sin gained a certain notoriety of no advantage to myself.

I mention these facts in order to show you in the first place that Huxley was, and is one of my heroes, and, secondly, to explain why I am so proud to find myself asked to recall his illustrious memory as a Huxley Lecturer of this Hospital. If I can do nothing else in this lecture than persuade some of my audience to devote a little of their time to reading Huxley's essays, I shall feel satisfied.

It is true that many of his teachings have now passed into common currency, and that most of his views on subjects at that time intensely controversial are accepted as a matter of course to-day, but nevertheless his essays are not only full of sense and knowledge, but most of them read as freshly now as when they were written, and form an example of the finest English literature ever written by a man of science. If there is anyone alive who still doubts whether a scientific training and outlook are incompatible with what is usually called culture, let him read and study Huxley's essays. Nowadays we hear much depreciation of the Victorian age, but some of us would like to see a few of the customs of that age restored. The modern young man and woman seem to provide for themselves little leisure for quiet reading or thought. I am persuaded that on account of this they miss much of the best in life. There is no better method of reminding them of their place in the world than that of reading Huxley's essays.

It is our special duty now, congregated as we are in Charing Cross Hospital, to remember that Huxley received his medical training here. He was, of course, no ordinary medical man ; he never practised, and even confessed that the treatment of disease had never interested him. He did, however, acknowledge that for one of his teachers, Wharton Jones, he had a higher regard than for any earlier or later teacher. This Hospital must be proud of the fact that it provided Huxley with much of the earlier training which made him a great scientific investigator and philosopher, even if it did not make him a great doctor. If he did not show any interest in actual medical practice, the same cannot be said of medical training and medical service. Anyone who reads his essays on " Elementary Instruction in Physiology " (1877), " On Medical Education " (1870), " The State and the Medical Profession," and " The Connection of the Biological Sciences with Medicine " (1881) will see what a tremendous influence he must have had in raising the status of medical education from a condition of chaos and absurdity to its present high level. With few exceptions, as, for instance, his advocacy of the unification of teaching of the so-called Institutes of Medicine (what we now call Chemistry, Physics and Biology) in one central Department of London University, practically all the suggestions and views he advanced have been adopted and passed into normal practice.

It must be puzzling to those who read the essays to notice how little space Huxley devotes to medical science as compared, for instance, with physical science. I think the explanation is that medical science had hardly been established in his day, and even the larger subject, biological science, was chiefly observational at that time. The result is that, when called upon to discuss scientific problems in general, he nearly always devoted most of his time to the physical sciences, the basis of which he grasped in an astonishing way. In 1887, in his essay on " Progress in Science," he writes of the firm foundation of the germ theory, and how it had supplied a scientific justification of vaccination, which had previously rested on an empirical basis : he refers also to the prevention and treatment of scabies : to the discovery of the cause of splenic fever (malaria) : to the freeing of England of plague by cleanliness and commonsense : to the promise of victory over hydrophobia ; and expresses the hope that diphtheria, typhoid and scarlet fevers will be similarly brought under control. In the essay, " Improving Natural Knowledge " (1866), he remarks that we have learned somewhat of Nature, we only partly obey her. " Because of this partial improvement of our natural knowledge and of that fractional obedience, we have no plague : because that knowledge is still very imperfect and that obedience yet incomplete, typhoid is our companion and cholera our visitor." He would have been interested to know that his prediction of the future incidence of these diseases has been fulfilled, and that our knowledge is not so imperfect and our obedience is more complete. We no longer see cholera, not even as a visitor, while typhoid is only a very rare companion, for, instead of killing 320 per million people in this country as it did in 1875, it is now only responsible for the death of about 4 per million per annum.

In his lecture to the British Association on " Biogenesis and Abiogenesis," delivered in 1870, he again shows his interest in the subject of infection and, although using silk-worm disease as one of his main illustrations, he mentions also two medical problems of similar nature. Thus, referring to Lister's work on the antiseptic method of treatment, he writes : " It appears to me impossible to rise from a perusal of those publications without a strong conviction that the lamentable mortality which so frequently dogs the footsteps of the most skilful operator and those deadly consequences of wounds and injuries which seem to haunt the very walls of great hospitals, and are even now destroying more men than die of bullet or bayonet, are due to the importation of minute organisms into wounds, and their increase and multiplication ; and that the surgeon who saves most lives will be he who best works out the practical consequences of the hypothesis of Redi." Redi was an Italian who was the first to give experimental proof that living matter always rises by the agency of pre-existing living matter. It must be remembered that, when Huxley referred to Lister's work in such approving terms, the germ theory of wound infection and antiseptic methods of Lister were by no means generally accepted. As late as 1877 Lister was not received with much appreciation when he joined the staff of King's College Hospital and found his lectures and his visits to the wards but sparsely attended by students. Surely Huxley would have rejoiced to see the general rise of antiseptic practice in surgery, and especially its logical development asepsis, and all this has meant to the well-being of mankind.

His second reference to medical problems in this lecture is to scarlet fever, of which he writes " Looking back no further than ten years it is possible to select three (1863, 1864 and 1869) in which the total number of deaths from scarlet fever alone amounted to 90,000. That is the return of killed, maimed and disabled being left out of sight." Then he adds his usual prophecy : " But the facts I have placed before you must leave the least sanguine without a doubt that the nature and the causes of this scourge will, one day, be as well understood as those of the Pébrine are now ; and that the long-suffered massacre of our innocents will come to an end." Now let us see what has happened to this disease since Huxley wrote those words. The organism has been isolated, its pathogenic activities determined, its toxins prepared and an antitoxic serum has been produced whose beneficial effects are undeniable. As for the killing power of this disease, its effects have diminished tremendously. Whereas in 1875 it was responsible for 720 deaths per million of the population, in 1934 this had been reduced to 20 per million. When Huxley referred to the maimed among the survivors of scarlet fever, he probably did not fully appreciate the ravages caused by this disease in the sequelae it leaves, especially middle-ear disease and nephritis. The mortality figures mentioned above are striking enough, but let me give you some of the latest figures resulting from the application of properly controlled and executed treatment by scarlet fever antitoxin.

In a series of cases during 1933 and 1934 suffering from scarlet fever under the care of Dr. H. S. Banks at the Park Hospital of the L.C.C., 1,877 received treatment by the intravenous injection of scarlet fever antitoxin, and 1,419 cases received no serum, being therefore regarded as controls. The tendency grew of admitting the severer cases to the ward for intravenous treatment when its beneficial effects were observed, so that the figures were rather weighted against the antitoxin receiving cases. In spite of this, they are very impressive.

Now let us see some of the results :—

	Cases	
	Antitoxin	*Control*
Number	1,877	1,419
Deaths	2	12
Average Stay in Hospital	18 days	33.9 days
Complications—		
Otitis media	35 (0.19%)	97 (0.68%)
Mastoiditis	1	7
Nephritis	4	25
Albuminuria	5	10
Broncho-pneumonia	2	11

I think Huxley would have been pleased with this modern scientific advance in the treatment of scarlet fever which he had predicted.

If Huxley came into this room and heard the present paean of praise, he would undoubtedly walk out. I propose now to recall him by some criticism—an action which would bring him running back, for he was always ready for combat when criticised. Fortunately, perhaps, for myself, any criticism I may offer will escape his sharp sword, but nevertheless it seems important at the present time to use this procedure to drive home my own firm belief in the one certain way for securing the rapid advancement of medical and other sciences, namely, the experimental method. I have grave doubts whether Huxley ever really appreciated the significance of the experimental method of investigation as a principle. It may be that he took it for granted, but since most of the great advance of knowledge in science in the past hundred years, especially in medical science, is directly due to experiment rather than to observation alone, it is surprising to me that Huxley, in such essays for instance as are found in his book called *Methods and Results* never specifies or uses the words " experimental method." In fact, the word " experiment " itself is almost missing. If this were the only criticism, it might still be thought that he took it for granted that " experimental method " was synonymous with " scientific research." But there are other pieces of evidence which suggest either that he did not like or that he did not appreciate the importance of the " experimental method." This can be seen, for instance, in his criticism of Francis Bacon, on whom he pours so much scorn, partly because in the " Novum Organum " Bacon gave as advantages of the experimental method the possibility of applying new discoveries to industry, and secondly " of procuring the superinducement of new forms of matter." It is true that Huxley hated the idea of pursuing knowledge for the sake of practical results, but both these criticisms have proved to be futile. The new knowledge gained by the experimental method has certainly had a tremendous effect, often beneficial, on industry, and if Huxley could return to earth and see the modern form of alchemy resulting from recent knowledge of the atom, he would realise the clear justification for Bacon's second suggestion and prophecy. The evidence, however, does not end there. No man received greater admiration from Huxley than Descartes. Besides the lecture, " Animal Automatism," which is almost entirely devoted to the work of Descartes, he wrote an essay in 1870 on Descartes' treatise entitled " Discourse touching the method of using one's reason rightly and of seeking scientific truth." He shows in this latter essay what most people will at once admit : " that the man who more than any other stands in the relation of such a stem (of a growing tree) towards the philosophy and the science of the modern world is René Descartes.'' But what teachings of Descartes are regarded nowadays as his most outstanding achievements? Is it only his view on the value of doubt and scepticism in science and the necessity of rigid truth? Or is it his philosophy which led on the one hand *via* Berkeley, Hume and Kant to idealism, and on the other by way of Priestley to modern physiology and materialism? It is, of course, none of these things alone. The teaching of Descartes that is now regarded as one of the most important of his philosophic contributions, is that he accepted, preached and practised the experimental method; and, as illustrating this, extolled the work of Harvey on the circulation of the blood as the royal road to discovery, and wrote the first text-book of physiology, *De l'Homme.* Now Huxley, so far as I can see, never mentions this aspect of Descartes' writings, except casually. He even says: '' The progress of physical science has been effected neither by Baconians nor by Cartesians as such, but by men like Galileo and Harvey, Boyle and Newton, who would have done their work just as well if neither Bacon nor Descartes had never propounded their views respecting the manner in which ' a scientific investigation ' should be pursued.'' This statement may or may not be true. Personally, I am inclined to think it is not true, especially in the case of physical science. As a matter of fact, even as regards physiology, Osler says that Richard Lower, Hooke and Hales were directly influenced by Descartes. This attitude of Huxley rather disturbs me. If he had been engaged all his life in a laboratory with his nose to the grindstone, one could have understood this point of view. But, as everybody knows, during much of his life Huxley did little active laboratory work, and his justification to greatness rests largely on his sane philosophising on scientific problems, including his writings on the methods and results of investigations made by others. Yet here he is scorning the particular views of his brother philosophers Bacon and Descartes, when, with wonderful foresight, they proclaimed the experimental method which has so transformed the world and man's outlook on it.

I wish to make it clear that I am referring here to the principle of the experimental method and not to any particular application of the principle. There is, of course, plenty of evidence that, when Huxley knew of work whose very nature was experiment, he was particularly appreciative. Nobody more greatly appreciated Harvey's experiments on the Circulation of the Blood, generally acknowledged as the first classical instance of the experimental method in biology, than Huxley; while his raptures over Pasteur's investigation in Silk-worm Disease, as described in his essay, '' Biogenesis and Abiogenesis,'' are noteworthy.

These briefly are the reasons for my doubting whether Huxley ever really appreciated what experiment means, and the fact that he refers occasionally to experiment as a method of scientific research does not upset this decision. Huxley himself was an investigator of the "observer" type, and it may be that it was this experience which prevented him from seeing the situation as expressed so well by the late Lord Moulton when he wrote : "Where we are reduced to observation, science crawls. Where and in proportion as you can use experiment, science advances rapidly." I have spent more time than I ought on these questions, but in defence I must plead that, in my opinion, the introduction and common use of the experimental method has been the greatest factor that I am aware of in "the Advance of Medical Science since Huxley's day," and I never cease to wonder why Huxley, with his penetrating mind, did not insist on the importance of this revolutionary phenomenon.

Most of the effective advance of medical science in Huxley's time centred round that branch of disease which is due to invasion of the body by micro-organisms, protozoal, bacterial and what we now know as virus. Some of these conditions have been referred to above. Their experimental and observational study has led to the elimination or control of many of these diseases, and to great advances in the subject of immunology and knowledge of the manner in which the body defends itself against pathogenic organisms and toxins. So successful was the study and so extensive the field that not only was the idea that all disease was caused by the invasion of the body by some *materies morbi* accepted, but the minds of men became resistant to the idea that other factors of an entirely different nature may be responsible for much ill-health. As an example of this suppressive effect of the all-conquering advance of the germ theory of disease may be mentioned the view advanced by Chatin that simple goitre was due to an iodine deficiency. It will be remembered that, so long ago as 1850, Chatin began his investigations into the distribution of iodine in foodstuffs, which led to the formulation of this view. In 1860 a Commission appointed by the French Academy of Science repudiated his hypothesis, with the result that the latter remained discredited until Baumann in 1895 discovered iodine in the thyroid gland. Thus died the first hypothesis of a deficiency disease.

One of the greatest triumphs of the experimental method during the present century has been not only to break down the resistance to this view of the invasive causation of all disease, but to establish on the firmest basis a view advanced by Claud Bernard in 1865—swamped for a long time by the successes of Pasteur, Lister and Koch and their followers—that many diseases are due to the abnormal working of processes which, when physiological, result in good health. On this basis it will be remembered that Bernard always claimed that medical science was Experimental Physiology. The discoveries in medical science that have brought us back to this view are, of course, those indicating (1) that much disease is due to the inharmonious action of internal secretions of many organs. To illustrate this group reference need only be made to the factors known to be responsible for such diseases as diabetes mellitus, diabetes insipidus, pernicious anaemia, exophthalmic goitre and other forms of hyperthyroidism, cretinism and myxoedema, Addison's disease, osteitis fibrosis cystica, acromegaly, and other diseases of the pituitary gland.

(2) That much disease is due to nutritional abnormalities, *e.g.*, rickets, osteomalacia, defective teeth and pyorrhoea, tetany, scurvy, beri-beri, pellagra, lathyrism, convulsive ergotism, several forms of nutritional anaemia, simple goitre, and diminished resistance to infection.

What we must recognise, I believe, is that these diseases by no means cover all the conditions which will be ultimately found to rest on similar causative factors. As they stand, however, they are impressive. It is also clear that the aetiological basis of both groups is of the same nature and indicates that departures from health are often due to the abnormal action of specific chemical substances. In the first group, these chemical agents are synthesised by the different organs and tissues of the body, either in excessive or deficient amounts, or under conditions when they cannot be properly effective. In the second group, the nutritional diseases are due to the absence from, or deficient supply to, the body of chemical agents which cannot be synthesised and must therefore be supplied in the food. Such substances include the vitamins and mineral substances necessary for life, and undoubtedly many other still unknown factors.

The general deduction that can be made from this advance in medical science is that health and disease are often different aspects of the same thing ; that when these innumerable chemical agents are present in the right amount and work in harmony, perfect health is found ; in unbalanced amounts and working inharmoniously, illness often of a specific nature develops. Here, then, is the strongest evidence of the so-called materialistic view—a description Huxley so energetically rejected—that the animal and human organism has a physical and chemical basis. Besides, therefore, giving to mankind wonderful power to prevent and cure many diseases, this type of knowledge, whose surface has only been scratched, affords support to a philosophic idea of the basis of life strongly advocated by the great man whose life we are commemorating to-day. He would have said that these discoveries of medicine show that " the further science advances, the more extensively and consistently will all the phenomena of nature be represented by materialistic formulae and symbols " (" Physical Basis of Life," 1868).

One of the most astonishing examples of chemical control of physiological functions is that recently seen in the results coming from many quarters of the world which show the diverse and yet associated activities of sterols in the animal body. Until a few years ago this group of substances had hardly been apportioned one function, but now we know a number of their extraordinary actions. It is realised, for instance, that such widely different substances as cholesterol, bile salts, ergosterol, vitamin D, the male hormone and the oestrogenic hormone from the ovarian follicles, are not only closely related chemically but in some cases have physiological and pathological actions in common. In this group we can also place the cancer-producing agents isolated by Kennaway, Cook and their colleagues. All these substances contain the phenanthrene ring, and differences in their biological effects are apparently due to the character of their side groups and the degree of hydrogenation. Many of their actions are shared by substances which have previously appeared widely remote. For instance, some of the tar products and their derivatives which produce cancer, *i.e.*, 1 : 2 benzpyrene and 5 : 6 cyclopenten-1 : 2 benzanthracene, are also oestrogenic. On the other hand, the oestrogenic hormone occasionally produces mammary cancer in male mice. Again, vitamin D, in addition to producing calcification of bones and teeth, also has an oestrogenic effect. Finally, we have the recent evidence that Spemann's " organiser "—the substance which is present in the blastopore and stimulates undifferentiated tissues of the embryo to form a second embryo is a sterol related to oestrin. There is an essential unifying effect in all this new knowledge of biochemistry, whether it is considered in its chemical or its biological aspect. When I also remind you that some of our most potent and useful drugs including the glucocides, strophanthin and digitalis, and the alkaloids morphine, codeine and colchine, also contain this phenanthrene grouping, you will see that we are immediately faced with the question, to which I shall refer later, namely, " Where is the border line between physiology, pathology and pharmacology? "

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In connection with this rapidly developing knowledge of sterol activity, some of the recently established facts of the action of the so-called sex-hormones seem to me to be the most suggestive of modern biological chemistry. I refer in particular to the action of the oestrin group in causing hypertrophy of the prostate in male animals, and in producing hernias by weakening the musculature of the abdominal wall. The question that at once suggests itself is whether we are not seeing " through a glass darkly " the possibilities that the changes of old age are related to unbalance of chemical elements of the body. When Huxley quoted with approval the following passage from Descartes : " We might escape an infinity of diseases of the mind, no less than of the body, and even perhaps of the weakness of old age if we had sufficient knowledge of their causes and of all the remedies with which nature has provided us," he little realised how near this stage of human knowledge might be.

If Huxley entered Charing Cross Hospital to-day he would see that a revolution had taken place in the diagnosis and treatment of disease. He would see many diseases, which in his day could not be controlled or cured, now amenable either to control or cure. Advances in knowledge of infective disorders and particularly of immunology would probably not surprise him because he had already appreciated the fact that there was a scientific basis to the prevention of smallpox by vaccination and to Pasteur's method of treating rabies. He would, however, undoubtedly be impressed with other great advances of medical science, often at the expense of medical art. He would see that large clinical laboratories and X-ray departments had developed in the hospital, and how rarely a patient leaves the hospital without having undergone some form of examination involving clinical pathology or X-ray examination.

Although the interpretation of the morbid condition in a patient and its best form of treatment by a physician still depends to a large extent on his past experience of similar cases, which forms so much of the art of medicine, diagnosis and treatment controlled by laboratory methods has become more and more prominent. Some regret this and say that the art of medicine is disappearing. This is true, but it seems to me useless to regret it. We must face the new situation, admit the growing importance of laboratory procedure, and realise that it is destined to become greater and greater. Why should we regret it? Surely it is only an additional weapon in the doctor's hands, and comparable in that respect with the introduction of the stethoscope by Laennec and percussion by Auenbrugger. The physician must make himself the master of these ancillary laboratory methods, as he has done in the case of the stethoscope, and at least be able to use them intelligently as instruments and evaluate their results. With the advance of medical science, symptomatic and empirical forms of treatment are diminishing, and there is a greater tendency to treat disease on fundamental lines necessitating a knowledge of the aetiology of the particular condition. There is, however, still a great but diminishing need for the practice of the art of medicine, and its importance will vary inversely as medical science progresses. Surely it is a good thing that the medical student coming into the wards for the first time should not be told, as he was within recent memory, to forget his physiology! All wise physicians nowadays recognise with Huxley that physiology is the basis both of pathology and pharmacology, that therapeutics is based on pharmacology, and that pathology and therapeutics largely make up the science of medicine. Listen to the following statement by Huxley: " From this point of view, pathology is the analogue of the theory of perturbation in astronomy: and therapeutics resolves itself into the discovery of the means by which a system of forces competent to eliminate any given perturbation may be introduced into the economy. And, as pathology bases itself upon normal physiology, so therapeutics rests on pharmacology: which is, strictly speaking, a part of the great biological topic of the influence of conditions on the living organism, and has no scientific foundation apart from physiology " (" Biological Science and Medicine ").

There is, however, something unsatisfactory at present about the training in medical science in universities. Huxley himself lived through the time when specialism in medical science developed. He saw Claud Bernard found the modern school of physiologists, Koch modern bacteriology, Virchow modern cellular pathology, and Lister modern surgery. Since his death specialism has become rampant, with the result that there is to-day no difficulty in finding biochemists, bacteriologists, morbid anatomists and other specialists. These, however, are not the men who as a rule open up new vistas by their discoveries. Such, usually, come from investigators of wide training who, while not experts in all these subjects, have sufficient knowledge of ~~difficult~~ technical differen methods to be able to use them as instruments so that, in considering how to investigate any particular problem with which they may be faced, they can command the right method of approach. I should like to see Universities make provision for the training of men with this equipment. This could be done by instituting an honours course covering biochemistry and the experimental sides of physiology, pathology and pharmacology. These subjects, so far as experimental medicine is concerned, could all be treated and co-ordinated as one study. By this means men with research ability would acquire a general view of the working of the body in health and disease, and would have control of the implements available for approaching the study of any problem from the most promising angle. They would also know the moment for calling in any particular specialist to their aid. It is needless to add that these men ought to be medically qualified and have a sound grasp of clinical medicine.

Having mentioned a few of the outstanding results obtained by the experimental method in the present century which obviously affect the general outlook on disease, I wish to refer to some other modern aspects of medical research. In my capacity as Secretary of the Medical Research Council it is my duty to assist this branch of activity in every way. Success in medical research depends to a large extent on the type of man attracted to such work. Men of the best type are limited in number, and cannot be appreciably increased by any known method. They must in general be what is known as clever men, but cleverness alone counts for little. In addition, they must be men of strong character, capable of hard and often disheartening work, with power to distinguish truth from falsehood, prepared to spend their lives with limited social contacts and to forego riches. It is clear that, when all these attributes are associated in one individual, you have something approaching a superman. Short of these rare finds, something can, of course, be done to attract able men, and by providing financial assistance and ensuring the proper kind of training, helping them to a career of medical research. This is one important aspect of the work of the Medical Research Council.

In recent years the Medical Research Council have announced a definite policy for advancing the study of Clinical Science by setting up special posts in the subject, when suitable men are obtainable. This policy has my hearty support, but I confess I am sometimes rather alarmed by the advocacy of some of its adherents. The claim that the subject of Clinical Science should be regarded as a discipline on its own, comparable in this respect to a subject such as, for instance, pathology, is certainly justifiable. If, however, the claim means, as it seems to mean to some of its advocates, that Clinical Science is to confine itself only to the study of diseases in man and cut itself off from the laboratory, I should regard this attitude with great regret. An isolationist policy in any single branch of medical science is retrograde, but in Clinical Science it is specially regrettable owing to the limited opportunities of using the experimental method on man. Apart from the discoveries waiting to be made in the natural history of disease by clinical observation, and even here laboratory methods of precision are often necessary, it seems to me that the future success of Clinical Science as a special subject must depend on its ability to use and develop methods of experiment. To refuse to go into the laboratory must limit the opportunities for experiment, and to this extent will undoubtedly cripple the advancement of the subject. No man engaged in scientific investigation can afford to scorn or disregard an implement which has proved so useful. I am an earnest advocate of combined clinical and laboratory work, and know from my own experience how beneficially the wards and the laboratory act and react in the mind of the investigator of medical problems, quite apart from the double facilities and opportunities afforded by such combined work.

There is one other aspect of medical research to which I wish to refer, namely, the question as to whether there is one special road more likely than others to lead to important discovery. There are some who boldly state that all *ad hoc* research on particular medical problems is useless, and that the only safe road is to work on some more or less academic subject without any hope of utility or application, and that the results obtained may or may not lead to discoveries of practical value. This is Huxley's view of research. There is, so far as I can see, no royal road to discovery in medicine. It may come by any method, from any quarter. Sometimes it comes by pure chance ; sometimes it is the reward of effort in the direction aimed at. What I am convinced of, however, is that, although important discoveries are rare and difficult to make in any case, it is no more unlikely that discoveries of first-class scientific interest will result from work directed to the solution of practical problems of disease than that discoveries of first-class interest to medicine will result from the study of academic physiological problems. When Huxley deprecated research undertaken to achieve practical results of utilitarian interest, he cannot have appreciated, so far as medical science is concerned, a point mentioned above, that disease in man is often simply abnormal physiology. It is not strange, therefore, that many instances can be given of research in recent years where the experimental study of a disease has resulted in the discovery of new physiological principles. Investigations on rickets led to the discovery of vitamin D and opened up a new chapter in the physiology of bones and teeth. The study of pernicious anaemia taught the physiologist the part played by the anti-anaemic principle of liver in the maturation of red-blood corpuscles. Similarly, the study of achylia gastrica promises to throw additional light on the physiology of the blood and nervous system. Again, experimental investigations relating to Addison's disease led to the discovery of the active principle of suprarenal cortex, whose physiological action is now being widely studied. Many other instances could be given.

I have discussed this aspect of medical research because I am convinced that more men ought to be prepared to study pathological and medical problems, as well as problems of physiology, by the experimental method. It is, however, essential that they should be equipped for both types of work and capable of interpreting their results in accordance with, and directing their attention to, any aspect, physiological or pathological, of the problem investigated. There is a tremendous field awaiting their intervention.

Huxley's interest in the nervous system was always great, especially as so much of his attention and energy was directed to questions of the human mind and to man's place in nature. It is with this aspect of his writings that I now wish to deal.

We can imagine him speculating and philosophising on the many astonishing facts that have come to light since his day, showing the specific actions of chemical agents normally present in the body in controlling the structure and function of the nervous system. In the light of these advances in knowledge he would, no doubt, read again his essays on " Animal Automatism," based on the writings of Descartes, and on the " Mental Phenomena of Animals " and on the " Contents of the Mind," and see whether it would be necessary to alter these or modify them in any degree. He would take into account the mind of the cretin and its great improvement following the administration of thyroxin. He would have to consider the interesting results of Dale and his colleagues whereby strong evidence was adduced to show that not only are chemical entities, acetyl choline and potassium ions, responsible for the transmission of the nervous impulse across the synapses of ganglion cells, but that a similar mechanism controls the discharge of the nervous impulse at motor nerve endings and most of the parasympathetic nerve endings. He would remember similar but earlier work, which suggested that adrenalin has a comparable function at most sympathetic nerve endings—that in general, nerve endings can be divided into cholinergic and adrenergic groups. He would further learn that cholinergic nerves can grow down and functionally replace other cholinergic nerves, and adrenergic nerves replace the other adrenergic nerves, but that cross-development and replacement cannot take place. He would remember that he had once written " With the progress of research, the term ' animal spirits ' gave way to ' nervous fluid,' and nervous fluid has now given way to ' molecular motion of nerve substance.' Modern results of research would no doubt impel him to add " and molecular motion of nerve substance has now been replaced by the chemical action of specific substances." On the whole, the articles on nervous phenomena, as written in 1874, stand unchallengeable, and the only effect of modern knowledge of the last thirty years is to reinforce and explain in greater detail in terms of chemistry his general view that " molecular changes in the brain are the causes of all the states of consciousness of brutes "— and indeed of man. He might indeed have ventured further, even into the field of prophecy, and said that it was no mere phantasy to suggest that in the near future much greater control of human nervous activity will be obtained by means of chemical substances having specific physiological action on nervous tissue.

In this regard I wish now to demonstrate by cinematograph one other series of facts showing the effect of chemical control of the nervous system. This is a subject I have been investigating for some years, especially the effect of certain diet ingredients, present in minute amounts, on the nervous system. I propose to demonstrate the fact that, if vitamin A is withheld from young growing animals, their nervous systems develop special defects which make their behaviour very abnormal. The first parts of the nervous system which degenerate under these conditions are practically confined to afferent nerves, including the optic, trigeminal, auditory and vestibular division of the eighth afferent nerves of the spinal cord and ascending fibres inside the cord up to the level of the Red Nucleus. Nerve fibres and cells related to the cerebellum are particularly involved. The presence of extremely small quantities of vitamin A or carotene of the order of a few milligrammes daily prevent these changes and, if developed, cures them if they have not proceeded too far.

You will see that in the case of animals deficient in vitamin A and/or carotene, the legs are stiff, the hind legs being specially affected. This is best seen in the dogs. These animals also move their heads in a curious and characteristic way, as if they did not know their position in relation to the rest of the body : sometimes the head is moved up and down and sometimes from side to side, and when at rest is often askew with ears awry. When they walk their movements resemble those of alcoholic intoxication. They may go round in circles, wobble from side to side, and in extreme cases fall over either to the side or backwards, sometimes being unable to regain the normal position. By way of contrast, you will notice that the control animals receiving exactly the same diet but with the addition of some source of vitamin A or carotene, or in some cases pure carotene in the diet, move about normally or nearly normally.

I had hoped to show you also a film illustrating the comparable effects of vitamin B_1 deficiency on the behaviour of birds, but this has proved impossible. This action is quite different from that of vitamin A deficiency, which usually takes months to develop, whereas B_1 deficiency is evident after a few weeks. The abnormal movements come on rapidly and intensively, and can usually be relieved at once by the administration of vitamin B_1. They are not due to degenerative changes in the nerve cells and fibres such as are found in vitamin A deficiency, but, as shown by Peters and his colleagues, to interference with the brain metabolic processes of such a kind that dextrose instead of being completely oxidised is changed only to pyruvic acid with the result that inco-ordination of nervous activity develops. A supply of vitamin B_1 usually restores both the metabolic process at fault and the resulting disorganised nervous function to normal very rapidly. Here, then, is further evidence of the truth of Huxley's philosophy concerning the physical and chemical mechanism of the nervous system. It can be said with assurance that this particular field of knowledge will be greatly enlarged in the near future.

I have now finished my task. I have done my best in the time available to remind you that Huxley was one of the greatest men of his age, that his understanding of the general principles underlying natural phenomena was exceptionally penetrating, and that his faith in science was unbounded. Modern advance in scientific knowledge and especially medical science has surely justified his words when he wrote : "I see no limit to the extent which intelligence and will, guided by sound principles of investigation and organised in common effort, may modify the conditions of existence."